# Movement During Sleep: Associations with Posttraumatic Stress Disorder, Nightmares, and Comorbid Panic Disorder

Steven H. Woodward, PhD;[1] Gregory A. Leskin, PhD;[1] and Javaid I. Sheikh, MD[1,2]

*[1]National Center for PTSD, Clinical Laboratory and Education Division, VA Palo Alto Health Care System, Palo Alto, CA; [2]Stanford University Medical School, Stanford University, Stanford, CA*

**Study Objectives:** To corroborate findings from the National Comorbidy study with objective sleep data.
**Design:** Retrospective data review.
**Setting:** Sleep Laboratory, National Center for Posttraumatic Stress Disorder
**Participants:** Male Vietnam combat veteran.
**Interventions:** N/A
**Measurements and Results:** We reanalyzed laboratory sleep data obtained from subjects undergoing inpatient treatment for posttraumatic stress disorder. Comorbid panic disorder was not associated with a significant worsening of objective sleep in this sample. Posttraumatic stress disorder, comorbid panic disorder, and trauma-related nightmare complaint were all associated with significant and systematic reductions of sleep movement time. Analyses of potential "rescoring" artifacts provided further support for this effect.
**Conclusions:** A curvilinear function may describe the relationship between anxiety symptom severity and sleep-movement time in both posttraumatic stress disorder and panic disorder. Evidence for movement suppression in association with pathologic levels of human anxiety is consistent with the suppression of movement ("freezing") exhibited by animals under conditions of perceived threat.
**Key words:** sleep, anxiety, panic, stress, traumatic

## INTRODUCTION

ANALYSES OF THE EPIDEMIOLOGIC DATA FROM THE NATIONAL COMORBIDY SURVEY[1] SUGGESTED THAT POSTTRAUMATIC STRESS DISORDER (PTSD) PATIENTS WITH COMORBID PANIC DISORDER (PD) EXPERIENCED ESPECIALLY HIGH RATES OF SLEEP AND NIGHTMARE DISTURBANCE.[2,3] Posttraumatic stress disorder and PD have much in common. Episodic hyperarousal is central to both disorders, and in both, dysregulation of $\alpha_2$ autoreceptors in the locus coeruleus has been hypothesized.[4-8] Mellman and Davis[9] have noted correspondences between the flashbacks of PTSD and the panic attacks of PD. Southwick et al[6] observed panic symptoms and flashbacks in PTSD patients under yohimbine challenge. Freed, Craske and Greher[10] reported high rates of trauma exposure in PD patients with nocturnal panic attacks. PTSD and PD are each characterized by subjective dyssomnia, that is, perceived difficulties in the initiation and maintenance of sleep.[11-13] In both disorders, subjective dyssomnia has not always been validated by modifications of sleep architecture.[12, 14] A substantial proportion of both PTSD and PD patients also experience parasomnias, or discrete aberrations of the sleep process. In both disorders, these take the form of paroxysmal arousals from sleep—trauma-related nightmares in PTSD, and nocturnal panic attacks in PD. In one study, approximately 33% of a PD outpatient sample "commonly" experienced nocturnal panic attacks,[15] while approximately 20% of the National Vietnam Veterans Readjustment Survey sample[16] reported frequent nightmares.[17]

At the same time, PTSD and PD are distinct clinical entities that should be demonstrable as involving distinct alterations of central fear systems. It can be further hypothesized that such alterations, to the extent that they are distinct, should be additive, and Leskin et al[2,3] may have found support for this possibility. They conducted secondary analyses of the National Comorbidity Survey data[18] in order to explore relations between PTSD comorbidity and sleep complaints. They found that nightmare complaints were significantly more elevated when PTSD was compounded by PD than when compounded by major depression (MDD), alcohol abuse/dependence (ETOH), non-alcohol substance abuse/dependence (SUBS), or generalized anxiety disorder. We sought to test the additivity of the effects of PTSD and PD on sleep by comparing the laboratory sleep of PTSD patients with and without comorbid PD. We expected to observe differences in sleep efficiency between PTSD patients with and without comorbid PD that mirrored the findings of Leskin et al. In brief, we did not. Instead, we observed previously unreported effects of PTSD, PD, and nightmare complaint on sleep movement, that is, the large-scale, temporally extended, positional adjustments that result in scorings of "movement time." Because these findings were in an unexpected direction, that is, more severe anxiety symptomology was associated with reduced movement time, and because we had adopted a convention of "rescoring" extended movement periods as "wake," a considerable portion of the following report relates our efforts to test the internal validity of these observations.

## METHODS AND MATERIALS

### Design

The design of this study was to compare laboratory sleep in PTSD with and without comorbid PD and controls.

### Subjects

All subjects gave written informed consent prior to participation in this study. Diagnoses of PTSD were determined through administration of the Clinician Administered PTSD Scale (CAPS;[19]). Male subjects were recruited from the PTSD Residential Rehabilitation Program and female subjects from the Women's Trauma Recovery Program at the Veterans Affairs Medical Center, Palo Alto (Menlo Park Division), California. Male subjects had been exposed to combat trauma in Vietnam, and female subjects, to a variety of victimization experiences during their military service. Patient recruitment was accomplished by word of mouth within the inpatient program. In all cases, referrals were reviewed and approved by attending psychiatrists who were familiar

**Disclosure Statement**
This research was funded by the Department of Veterans Affairs.

**Submitted for publication September 2001**
**Accepted for publication April 2002**
Address correspondence to: Steven H. Woodward, Ph.D., Sleep Laboratory, National Center for PTSD, VAPAHCS, Bldg. 352, 795 Willow Rd., Menlo Park, CA 94025; Fax: 650-617-2684; E-mail: steve.woodward@med.va.gov

**Table 1a:** Psychometric data from study participants

| | CONTROL | PTSD-PD | PTSD+PD | | |
|---|---|---|---|---|---|
| | % | % | % | $x^2$ | *p* |
| History of MDD | 26 | 86 | 83 | 0.17 | n.s. |
| Current MDD | 0 | 65 | 65 | 0.002 | n.s. |
| ETOH | 9 | 72 | 70 | 0.06 | n.s. |
| SUBS | 9 | 61 | 59 | 0.03 | n.s. |

**Table 1b:** Psychometric data from combat-exposed subjects

| | CONTROL | | PTSD-PD | | PTSD+PD | | | |
|---|---|---|---|---|---|---|---|---|
| | mean | sd | mean | sd | mean | sd | *t* | *p* |
| CAPS Total Severity | 25 | 21 | 81 | 14 | 89 | 23 | 2.06 | 0.04 |
| Mississippi Scale | 86 | 26 | 122 | 15 | 121 | 14 | 2.17 | 0.03 |
| Combat Exposure Scale | 23 | 9 | 27 | 8 | 30 | 8 | 1.60 | 0.11 |
| Beck Depression Inventory | 7 | 8 | 25 | 10 | 26 | 9 | 0.36 | n.s. |

with the prospective subjects and who also directly supervised any subsequent medication washout. As a group, inpatient subjects entering laboratory studies at our facility exhibit slightly less-severe PTSD than the inpatient sample from which they are drawn, with specific reductions in nightmare severity, exogenous cue avoidance, and sense of foreshortened future.[20] Controls were recruited from the community using a variety of means, including print advertisements and workshops provided for veterans' organizations. All subjects were pre-screened for medical disease and chronic pain that could influence sleep, obvious risk factors for obstructive sleep apnea (frequent snoring, obesity, or partner reports of interrupted breathing during sleep), or a recent history of heavy alcohol use (intake greater than 5 oz. per day for any 30-consecutive-day period during the preceding 6 months). Subjects were later excluded if, on any laboratory night, they exhibited an apnea/hypopnea index greater than 10 events per hour. The final sample consisted of 88 PTSD inpatients (84 males/4 females, mean age 45.8 years, s.d. = 2.4), and 23 community-residing controls (16 males/7 females, mean age 44.8 years, s.d. = 1.9).

Comorbid diagnoses were determined through administration of the Structured Clinical Interview for the DSM-IV (SCID[21]); and were common among patients. Twenty-six percent of patients (n = 23) met criteria for current PD, 85% for recurrent major depressive disorder (MDD), 64% for current MDD, 72% for history of alcohol abuse or dependence (ETOH), and 61% for history of substance abuse or dependence (SUBS). Comparative rates of comorbidity and PTSD-related symptomology for the PTSD+PD group, PTSD-PD group, and controls are presented in Tables 1a,b. This pair of tables presents psychometric data obtained from the control, PTSD-PD, and PTSD+PD groups. Statistical tests reported in the right hand columns apply to comparisons of the PTSD-PD and PTSD+PD patient groups. In Table 1b, all control values represent means of combat exposed subjects only, with the exception of the BDI, which was obtained from all subjects.The PTSD+PD and PTSD-PD groups were closely matched on rates of comorbid diagnosis. (Four patients were missing SUBS diagnoses.) Patients with PTSD+PD exhibited mild elevations in estimates of overall PTSD severity relative to the PTSD-PD patients; however, their reported combat exposures were also slightly higher. Dysphoria as indexed by the BDI did not distinguish PTSD patients with and without comorbid PD. Patients with and without PD differed in endorsements of subjective sleep difficulties only in the realm of nightmare disturbance. Patients with PTSD+PD endorsed more nightmares on the CAPS [4.8 vs. 3.2, t(79) = 2.40, p = 0.019] and tended to exhibit higher scores on a nightmare item extracted from the MISS (sum of items 7 and 14; 6.9 vs. 6.1, t(79) = 1.70, p = 0.098). Patients with PTSD and recurrent MDD complained of more difficulty initiating and maintaining sleep on the CAPS [6.1 vs. 4.8, t(79) = 2.39, p = 0.019], but not more nightmare disturbance, than those without recurrent MDD. In this sample, neither ETOH nor SUBS was associated with effects on subjective sleep. Among controls, 4% (1) met criteria for current PD, 26% for recurrent MDD, none for current MDD, 9% for ETOH, and 9% for SUBS.

History of nightmare complaints was assessed via a sleep history questionnaire.[22] Seventy-eight percent of the PTSD-PD, 82% of the PTSD+PD patients, and 17% of the combat-exposed controls endorsed a history of trauma-related nightmares occurring at least monthly. Seventy percent of the PTSD-PD, 59% of the PTSD+PD patients, and 25% of the combat-exposed controls endorsed a history of non-trauma-related nightmares occurring at least monthly. None of the non-combat-exposed controls endorsed a history of nightmares.

All subjects had been abstinent from alcohol for at least 60 days prior to polysomnographic testing. Sixty-seven patients had been free of sleep-modifying prescription medications for at least 2 months prior to the study. The remaining 21 patients and 1 control were studied after monitored withdrawal from psychotropic medications for periods exceeding 4 elimination half-lives.

### Procedures

Subjects slept 2, 3, or 4 nights in the sleep laboratory (numbers of subjects spending 2, 3, or 4 nights in the lab were 4, 40, and 67, respectively) located within the inpatient unit. The number of study nights varied largely as a function of technician availability and patients' schedules. Scheduling was arranged to accommodate subjects' typical bed times. Inpatient subjects terminated their sleep at will, but not later than 6:00 AM, the standard wake-up time for the inpatient treatment program. Subjects had resided in the program for an average of 36 days. The recording montage included two channels of bipolar electrooculogram (EOG, vertical and horizontal derivations), four channels of scalp electroencephalogram (EEG; F3, F4, Cz, and Pz referred to linked mastoids), mentalis and left anterior tibialis electromyograms (EMG), abdominal respiratory effort, electrocardiogram (ECG), and blood oxygen saturation. The ECG was recorded using the "lead 1" derivation and filtered to 1 to 30 Hz prior to digitization. The EOG and EEG were filtered to a 0.3 to 30 Hz bandwidth. The EMG was filtered to a 30 to 300 Hz bandwidth, then rectified and integrated over a 20-millisecond time-constant. After conditioning, all physiologic data were digitized at 125 Hz and streamed to disk. Manual sleep staging of paper records was performed by trained sleep technicians following standard criteria applied to 30-second epochs. The EEG from the Cz site was used for sleep staging. Indices of sleep architecture extracted included time asleep, time in stages 1, 2, 3, 4, and rapid-eye movement (REM) sleep, wake, movement time (MT), and latencies to sleep and to REM sleep. Sleep latency was measured from lights out to sleep onset defined by the appearance of three consecutive epochs of sleep. The REM sleep latency was measured from sleep onset to the appearance of three consecutive epochs of REM sleep.

### Movement Time Scoring

The criteria for scoring MT will be described in detail as they figure prominently in what follows. The MT was scored when more than half an epoch contained dense, large-amplitude artifacts in EEG, EOG, and EMG channels.[23] We observed the additional convention that when contiguous epochs met criteria for MT, only the first received an MT designation, while the remainder were scored as wake. Figure 1 plots a summary of the 1800+ MT events scored in this study. The aggregate probabilities (over all subjects and nights) of stages 1-4, REM, wake, and MT are plotted per 30-second epoch for 15 minutes before and after MT. This figure confirms that MT scorings were, as required by the employed conventions, solitary events. A mild reduction in NREM in favor of REM sleep is discernable as the MT epoch approaches, as well as a steeper increase in the probability of stage 1 sleep in the final few minutes prior to a MT epoch. Stage 1 sleep accounted for most of the sleep immediately following movements. The data presented in Figure 1 were recombined and aggregated over time to yield per subject per night probabilities for stages 1-4, REM, and wake for the 15 minutes before and after MT epochs for nights one and two. (For this analysis,

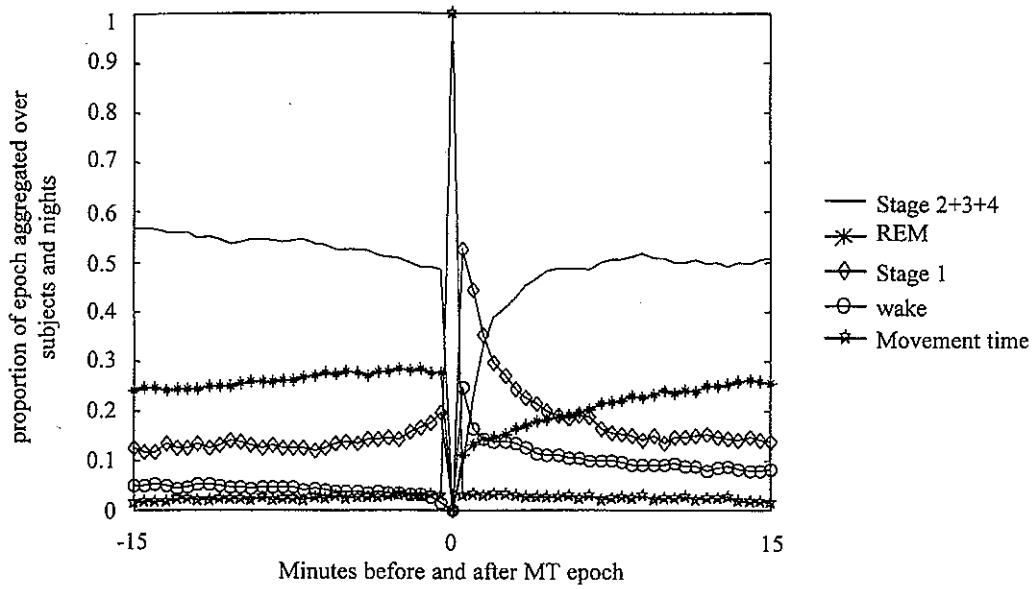


**Figure 1**—Plot of sleep staging before and after movement time (MT)-scored epochs, aggregated over all subjects and nights. The plot indicates the solitary character of MT epochs. Note also mild decrease in probability of NREM (stages 2+3+4) and mild increase in probability of REM prior to MT epochs, as well as a sharper increase in the probability of stage 1 just before. MT epochs were followed initially by stage 1 sleep, with normal stage distributions in place by 15 minutes after MT.

MT epochs were excluded if they fell within 15 minutes of lights out, lights on, and intercurrent out-of-bed episodes. Application of these criteria resulted in the loss of approximately 33% of subjects.) The distribution of sleep to stages in the 15 minutes prior to MT epochs (stage 1;11%, stages 2+3+4;56%, REM;26%) was stable over nights and closely mirrored all-night percentages. This analysis confirmed indications from Figure 1 that no clear prodrome preceded MT epochs.

Between-group differences were analyzed with ANOVA and Fisher's LSD, and relations between sleep measures and symptom severity measures with Pearson product-moment correlation coefficients or Spearman's rho. Associations between MT and indices of waking were analyzed using multiple regression.

## RESULTS

As presented in Table 2, conventional sleep architecture indices generally did not distinguish among controls, PTSD-PD patients, and PTSD+PD patients. The single, strong counterexample to this pattern was MT. Both raw MT ($F(2,108) = 7.34$, $p = 0.001$), and MT expressed as a percentage of the sleep period ($F(2,108) = 7.60$, $p = 0.001$; See Fig. 2), exhibited a monotonic decline over controls, PTSD patients with, and PTSD patients without panic symptomology. Tested via Fisher's LSD, all pair-wise comparisons were also significant. Though not shown, mean percentage of MT in the total sleep period in PTSD patients with panic attacks only was intermediate between values for PTSD patients with and without full PD.

### Comorbidity Analyses

Because chronic severe PTSD is typically accompanied by comorbid MDD, ETOH, SUBS, or a combination of these associations between these diagnoses and MT (calculated as a percentage of the sleep period) were evaluated as cell sizes permitted. (None of the controls were currently depressed and only two had histories of either ETOH or SUBS.) Recurrent MDD, crossed with the full control/PTSD-PD/PTSD+PD grouping factor was also found to be associated with an effect on MT [$F(1,105) = 5.11$, $p = 0.026$], but, in contrast to PTSD, was associated with elevated MT. As the two factors did not interact [$F(2,105) = 0.38$, ns], the effect of the Control/PTSD-PD/PTSD+PD grouping factor was further strengthened [$F(1,105) = 9.11$, $p = 0.0002$]. Effects of current MDD, ETOH, and SUBS were evaluated within the patient sample only. Unlike recurrent MDD, current MDD was not associated with a main effect on sleep MT [$F(1,84) = 0.35$, ns], and did not interact with the presence or absence of PD [$F(1,84) = 0.07$, ns]. Considering these findings together, it is apparent that they derive from especially low sleep MT levels in PTSD+PD subjects without histories of MDD. Tested in a similar fashion, neither a history of ETOH nor of SUBS was associated with an effect on sleep MT [$F(1,84) = 0.40$, ns; $F(1,80) = 0.45$, ns, respectively]. Neither ETOH nor SUBS interacted with the presence or absence of PD [$F(1,84) = 0.004$, ns; $F(1,80) = 0.01$, ns, respectively].

Subjects with PTSD were next classified according to whether or not they endorsed trauma-related and or non-trauma-related nightmares on the sleep history questionnaire. An ANOVA crossing these factors found the effect of the former to be significant [$F(1,67) = 7.9$, $p = 0.006$], while the effect of the latter was not [$F(1,67) = 0.91$, ns]. The two factors did not interact [$F(1,67) = 0.70$, ns]. This pattern was in accordance with prior observations that trauma-related but not non-trauma-related nightmares demonstrate associations with objective sleep variables.[22] When the presence or absence of trauma-related nightmare complaint was crossed with presence or absence of PD, both effects were weakened, suggesting they overlapped [trauma-related nightmares: $F(1,67) = 3.44$, $p = 0.07$; comorbid PD: $F(1,67) = 4.93$, $p = 0.03$]. Trauma-related nightmare complaint and PD did not interact.

Further confirming the trend toward lower MT in association with trauma-related nightmares, MT was strongly and inversely correlated with the MISS nightmare factor [$r(79) = -0.357$, $p < 0.001$]. In contrast, sleep MT was not correlated with the MISS sleep initiation or maintenance factor [$r(79) = -0.093$, ns]. This pattern of findings is noteworthy in that these two MISS factors are themselves highly intercorrelated [$r(79) = 0.61$, $p < 0.001$]. Inspection of scatterplots ruled out contributions from outliers to this result. The relationship between sleep MT and MISS total score was also insignificant [$r(79) = -0.112$, ns].

**Table 2.**

| | CONTROL | | PTSD-PD | | PTSD+PD | | | |
|---|---|---|---|---|---|---|---|---|
| | mean | SD | mean | SD | mean | SD | F | *P* |
| Lights out | 23:17 | 43 | 23:02 | 57 | 23:02 | 57 | 0.18 | n.s. |
| Minutes Asleep | 337.6 | 44.3 | 344.0 | 50.7 | 338.8 | 53.3 | 0.19 | n.s. |
| Sleep Efficiency | 90.8 | 4.5 | 91.8 | 4.2 | 90.8 | 5.9 | 0.60 | n.s. |
| Sleep Latency (min) | 8.5 | 7.9 | 7.1 | 5.4 | 7.2 | 5.1 | 0.52 | n.s. |
| Wake after Sleep Onset | 24.0 | 15.0 | 23.5 | 17.8 | 28.7 | 21.5 | 0.71 | n.s. |
| STAGE 1 (min) | 38.9 | 19.4 | 39.5 | 20.3 | 37.2 | 11.0 | 0.11 | n.s. |
| STAGE 2 (min) | 180.7 | 43.7 | 186.8 | 45.5 | 173.3 | 50.9 | 1.58 | n.s. |
| SWS (min) | 29.8 | 25.0 | 26.8 | 23.8 | 29.0 | 9.1 | 2.90 | n.s. |
| REM (min) | 88.3 | 24.0 | 89.4 | 23.1 | 92.1 | 26.8 | 1.34 | n.s. |
| REM latency (min) | 73.2 | 20.7 | 64.8 | 28.0 | 66.2 | 23.3 | 0.91 | n.s. |
| **Movement Time (MT)** | **3.0** | **3.0** | **1.9** | **2.2** | **0.5** | **1.0** | **7.34** | **0.001** |

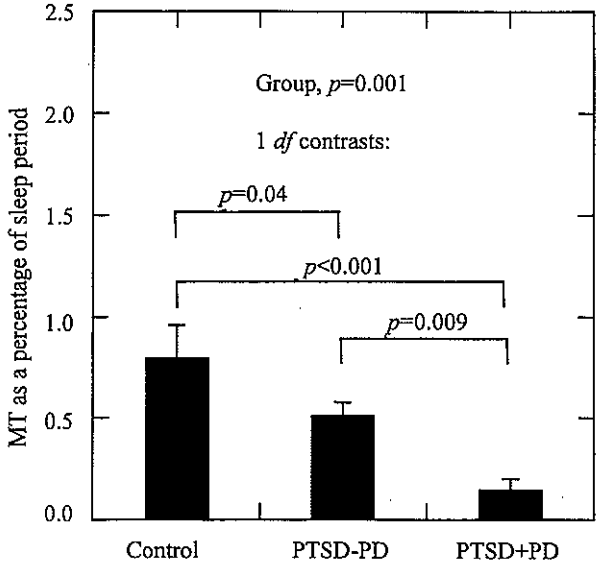


**Figure 2**—Plot of means and standard errors of MT expressed as a percentage of the total sleep period over controls, combat-related PTSD-PD patients without symptoms of PD, and PTSD+PD patients with full PD. Significance levels shown correspond to the main effect of group and to 1 *df* contrasts assessed with Fisher's LSD test.

### Tests of Internal Validity

Additional analyses were performed to test the internal validity of the observed effects on MT. It was first considered whether our laboratory's sleep-scoring conventions could have resulted in artifactual group differences in MT. A difference in the duration of post-MT wake episodes favoring patients could indicate that they had fewer, but longer, episodes of rescored MT rather than real differences in MT. The mean duration of wake following MT scorings was calculated per subject per night for nights one through three, then averaged over nights. (This value was not calculated for 33 subjects missing MT scorings on any of those nights.) There was a significant effect of the control/PTSD-PD/PTSD+PD grouping factor on the length of post-MT wake [$F(2,75) = 3.1$, $p = 0.049$]; however, this effect was one of monotonic decrease in the mean length of post-MT wake over the control, PTSD-PD, and PTSD+PD groups (47.4 vs. 21.8 vs. 9.5 seconds, respectively). That is, rescoring continuing movement as wake was unlikely to have created the observed group effects. Instead, the patient groups probably exhibited not only fewer, but briefer, MT episodes. The main effect of the control/PTSD-PD/PTSD+PD grouping factor remained highly significant in the subset of subjects with nonzero MT on nights one through three [$F(2,75) = 7.34$, $p = 0.001$].

It was also of interest to explore the temporal association between MT and waking without requiring that the latter be contiguous with the MT epoch. This analysis was performed on the data presented in Figure 1, recombined and aggregated over time to yield per subject per night probabilities for wake for the 15 minutes before and after MT epochs for nights 1 and 2. (As in the prodrome analysis, strict inclusion criteria for MT epochs for this analysis resulted in the loss of approximately 33% of subjects.) Again, peri-MT waking exhibited a monotonic association with the Control/PTSD-PD/PTSD+PD grouping factor [$F(2,75) = 3.2$, $p = 0.046$]. As depicted in Figure 3, controls exhibited the most waking in the vicinity of MT epochs, followed by PTSD-PD patients and then PTSD+PD patients. Also apparent in Figure 3 is a near-significant interaction of group and period reflecting the fact that group differences were limited to the post-MT period [$F(2,75) = 2.92$, $p = 0.06$].

We next reasoned that subjects exhibiting more wake episodes would have more opportunities for MT scoring since only the first epoch of a movement episode would be scoreable as MT. Accordingly, we compared the total number of wake episodes across groups. The control/PTSD-PD/PTSD+PD grouping factor was associated with a monotonic effect on the number of wake episodes [$F(2,108) = 3.37$, $p = 0.029$], with PTSD+PD patients exhibiting the most wake episodes and PTSD-PD patients the fewest. The pair-wise comparison between PTSD patients with and without PD was also significant [$F(1,108) = 6.0$, $p = 0.016$]. This pattern was also preserved when the number of wake episodes was residualized by linear regression on wake after sleep onset [$F(2,108) = 2.96$, $p = 0.056$] in order to account for any group differences in the total amount of wake episodes. In summary, the subject group with fewest MT epochs, the PTSD+PD sample, had the most opportunities for such scorings.

In the course of the latter analysis, it was observed that over all subjects the correlation between MT and number of wake episodes was negative and significant [$r(109)=-0.41$, $p = 0.000006$; residualized wake episodes: $r(109)=-0.38$]. Evaluating the controls separately, this relationship remained negative and significant [$rho(21) = -0.51$, $p < 0.02$]. The complementary correlation between MT and median duration of wake episodes was also positive and significant [$r(109) = 0.37$, $p = 0.00006$; in controls evaluated separately: $rho(21) = 0.45$, $p < 0.045$]. In other words, sleep MT was more strongly related to the structure than to the amount of waking. This was further confirmed by a multiple regression of sleep MT on number of wake episodes, duration of wake episodes, and wake after sleep onset, which yielded standardized beta weights of $b = -0.38$ ($p = 0.001$), 0.18 ($p = 0.06$), and 0.16 ($p = 0.11$), respectively. (It is likely that the relative sizes of the beta weights for number and duration of wake epochs are biased toward the former by range restriction in the latter, as 95% of all wake episodes were less than 4 minutes in length.)

### Relation of Movement Time to Other Features of Sleep

We considered whether group differences in MT could reflect differential adaptation in this sleep parameter over nights in the laboratory. Over all subjects, adaptation of MT over nights 1 through 3 was not significant [$F(2,210) = 0.29$, ns]. Five subjects were deleted from this analysis because of missing data from night 1 or night 3 and did not interact with the control/PTSD-PD/PTSD+PD grouping factor [$F(4,206) = 0.43$, ns]. However, adaptation in MT interacted with trauma-related nightmare complaint in the following manner. Patients who did not endorse trauma-related nightmares (n=15) exhibited increased MT over nights,

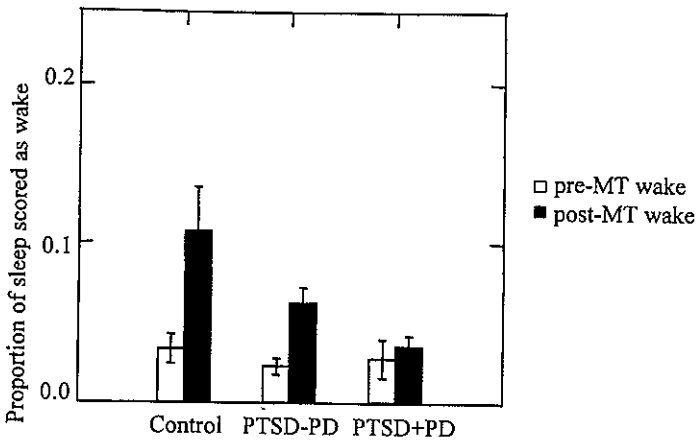


**Figure 3**—Proportions of sleep scored as wake 15 minutes before and after MT epochs across controls, PTSD-PD, and PTSD+PD groups. The MT was more closely associated with waking in controls than in PTSD patients with and without PD.

whereas patients who endorsed trauma-related nightmares did not [n = 52; $F(2,130) = 4.1$, $p = 0.020$, Huynh-Feldt correction, $e = 0.96$; See Figure 4]. Controls also did not exhibit significant adaptation in MT [$F(2,44) = 0.40$, ns].

Like Horne et al,[24] we observed an inverse relationship between MT and indices of slowwave sleep values (SWS) ($r = -0.170$ to $-0.273$, all $p < 0.05$). However, the pattern was much weaker here than in Horne's data and did not distinguish patients from controls, PTSD patients with or without comorbid PD, or PTSD patients with or without trauma-related nightmare complaint. In fact, since SWS was nonsignificantly reduced in patients versus controls, in PTSD patients with versus those without comorbid PD, and in PTSD patients with versus those without trauma-related nightmare complaint, the addition of SWS percentage as a covariate had the consequence of strengthening all of the corresponding effects upon MT.

Sleep MT exhibited no relationship with sleep efficiency [$r(109) = -0.04$, ns], but did exhibit a just-significant inverse correlation with wake after sleep onset [$r(109) = -0.19$, $p = 0.045$]. While not a strong effect, this observation represents another violation of the supposition that MT indexes impairment of sleep.[25]

## DISCUSSION

This study was motivated by an epidemiologic finding indicating that sleep and nightmare symptomology are elevated in PTSD when compounded by PD.[2] We did not observe a modification of gross laboratory sleep architecture in PTSD patients as a function of comorbid PD status. While this study found that comorbid PD was associated with an intriguing pattern of reduced large-scale movement during sleep, this effect is difficult to construe as indicative of worsened sleep. The MT accounted for only a small percentage of time-in-bed and was unrelated to difficulties in sleep initiation and maintenance. On the other hand, as reduced MT was strongly associated with nightmare complaint, the "hallmark" of PTSD,[26] and with more frequent arousals, it is equally unlikely to have indicated better sleep. Particularly intriguing, in this context, is the earlier report by Lavie and Hertz[25] that a small sample of "combat neurotics" exhibited a positive correlation between MT and sleep efficiency.

In this light, we briefly review what is known about the functional significance of sleep MT.

As noted, MT is scored when more than half an epoch contains dense, large-amplitude artifacts in EEG, EOG, and EMG channels.[23] As a result of the duration criterion, an MT scoring most often corresponds to an episode of whole-body movement resulting in a new sleeping position.[27] One function for such position changes is suggested by the fact that their absence, as in Parkinson disease, puts sleepers at risk for decubitus ulcers.[28] From this perspective, at least, less MT does not equate to better sleep; rather, some amount of whole-body movement during the night appears critical to maintain soft-tissue perfusion. The MT is to be distinguished from brief limb and body movements that are 10 to 20 times as frequent and highly discriminative of sleep stage.[24,29] In fact, the relationship between these two "compartments" of sleep movement appears wholly unknown. Only a few studies have measured small limb and body movements and conventional MT concurrently,[24,29,30] and none have analyzed their covariance. Preliminarily, we have also observed no covariance between sleep MT and leg-EMG burst activity aggregated over the night, another metric of sleep motor activity presumably related to small limb and body movements (Woodward et al, in preparation). These preliminary observations suggest that reduced MT in PTSD is not incompatible with earlier reports of elevated REM-phasic motor activity in PTSD.[31]

One of the few conditions, somatic or psychiatric, associated with modification of sleep MT is PD. Initial studies pointed to elevation of MT in PD;[32-34] however, further investigations have suggested a more complex picture. In studying PD patients with nocturnal panic attacks, Mellman and Uhde[11] observed that patients exhibiting nocturnal panic attacks in the laboratory had the lowest MT, while patients not exhibiting such attacks in the laboratory had the highest MT. Relatedly, there was a trend for patients with nocturnal panic attacks to exhibit reduced MT on those nights when their attacks occurred. This pattern led Uhde[15] to suggest that increased movement during sleep might protect against nocturnal panic attacks. Further insight into the relationship between PD symptoms and sleep MT is provided by the observations of Clark et al[35] who performed 24-hour ambulatory heart-rate and movement monitoring in 64 PD patients. Although they recorded movement primarily to ensure valid comparisons of heart rates, these authors made the unexpected observation that movement was reduced below control levels in PD patients with high agoraphobic avoidance and elevated above control levels in PD patients with low agoraphobic avoidance. This pattern led to a significant inverse relationship between trait anxiety and movement over all patients. The results of these two studies appear formally similar if it can be assumed that PD patients with nocturnal panic attacks experience more central fear-system activation during sleep than those without, and PD patients with high agoraphobic avoidance experience more central fear-system activation than patients with low agoraphobic avoidance. In both cases, patients with relatively less pathologic anxiety exhibited more movement than controls, while those with more relatively pathologic anxiety exhibited less.

While data suggesting that anxiety could be associated with reduced or suppressed movement run contrary to our expectations that agitation and restlessness usually accompany anxiety in humans, they are wholly consistent with a canonic defense response, movement suppression or "freezing." Freezing is among the strongly conserved behavioral outputs of amygdalar fear systems,[36] the first and lowest-threshold response to feared contexts in most animals,[37-39] and, interestingly, the only fear response not motorically incompatible with sleep. Our naive expectations of a positive relationship between anxiety and movement in humans may be conditioned by exposure to nonpathologic levels of anxiety, while the negative relationship may apply specifically to variation over more pathologic levels of anxiety. As Clark et al themselves suggest, the combination of these functions yields a familiar "inverted-U"-shaped curve characteristic of many relationships involving arousal.[35]

How does this framework fare in organizing the data collected in this study? Here, it was observed that PTSD patients both with and without comorbid PD or trauma-related nightmares exhibited reduced MT as compared to controls. This is not necessarily incompatible with a quadratic function relating anxiety symptoms to movement, as our sample of chronic severe combat-related PTSD inpatients may have repre-

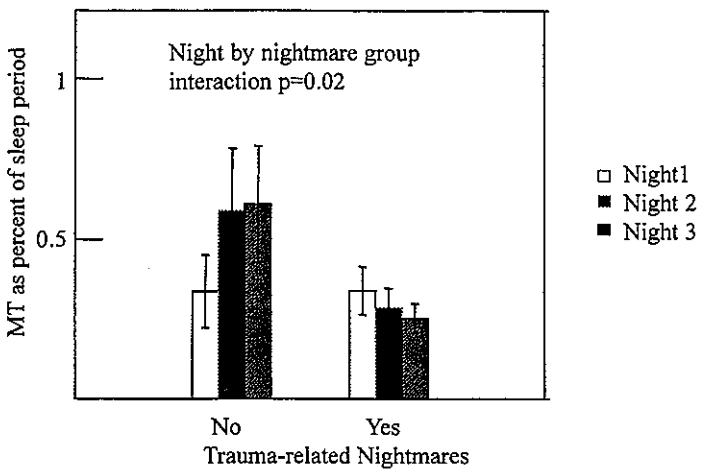


**Figure 4**—Movement time (MT) in minutes on nights 1, 2, and 3 in the sleep laboratory in combat-related posttraumatic stress disorder (PTSD) patients with and without trauma-related nightmare complaint. Note effect of nightmare complaint on both over all levels of MT and adaptation of MT over nights.

sented only highly pathologic levels of anxiety. However, if such was the case, any increments in syndrome severity consistent with elevated central fear-system activation should have resulted in reductions in movement. In fact, comorbid PD and trauma-related nightmare complaint were both associated with significant reductions in sleep MT. Conversely, adaptation to the laboratory, a familiarization process presumably associated with reduction of contextual fear, was associated with increased MT, at least in PTSD subjects without trauma-related nightmare complaints. Interestingly, non-trauma-related nightmare complaint was not associated with reductions in sleep MT in PTSD patients, implying that non-trauma-related nightmares do not index anxiety and central fear-system activation, or do so differently than trauma-related nightmares. This last observation augments other indications that trauma-related and non-trauma-related nightmare complaints have distinct associations with sleep behavior in PTSD.[40,41]

These data remain in conflict with self-reports of "thrashing, violent movements" during sleep obtained from PTSD patients[42]; however, in the rare instances when such episodes have been observed in the laboratory, they have been associated with relatively recent trauma.[43] It is perhaps relevant that our subjects were studied more than 20 years after their combat experiences. Lavie et al[44] have hypothesized contrasting acute and chronic phases of sleep disturbance accompanying PTSD following trauma. Their data indicate that the chronic phase includes elevated arousal thresholds to neutral stimuli, a counterintuitive feature which, like reduced MT, invites interpretation as evidence of undisturbed sleep. An analysis of the covariance of sleep MT and arousal thresholds in PTSD may prove illuminating. It is not clear whether the current findings of reduced MT contradict the report of Dagan et al[45] that actigraphically recorded sleep fails to distinguish PTSD patients from controls. Conventional actigraphy aimed at sleep-wake discrimination, which Dagan's study employed, cannot distinguish small brief limb and body movements from the large-scale position changes comprising MT. Such discrimination requires actigraphic recording of movement intensities (rather than simple counts) with high temporal precision (eg 1 second sample period). Such recordings have only recently become possible due to increased actigraph storage capacity. Parenthetically, our data appear to support the inadvisability of depending solely upon actigraphy to estimate sleep in clinical populations unless the sleep/wake scoring algorithm employed has demonstrated validity in the diagnostic group under study. Algorithms now in use have derived from concurrent actigraphic and polysomnographic studies performed in normals[30,46]; however, it has been shown that at least one such algorithm was invalid when applied to a depressed sample.[47] In the current study, the two diagnostic groups differed in the probability of wake in the vicinity of an MT epoch, implying that whole-body movements could "predict" waking better in controls than in patients. The same may apply to the small brief movements more closely tied to sleep depth.[29]

If the proposed analogy between reduced waking and sleep movement in humans and movement suppression in laboratory species proves valid, it may provide a new and important link between human and animal studies of fear. Interaction between central sleep and fear mechanisms is predictable on neuroanatomic grounds,[48] and has recently been confirmed in a study demonstrating that macaques with lesions of the amygdala display fewer brief awakenings and higher REM percentages than do unoperated animals.[49] Functional imaging studies have suggested that PTSD is characterized by disinhibition of the amygdala through compromise of ventromedial cortical influence over that structure.[50,51] A sleep pattern characterized by relative immobility and frequent brief awakenings appears compatible with the possibility of hyperactivated or disinhibited aymgdala in PTSD. Efforts to understand the role of the amygdala in mediating the effects of stress on sleep in other laboratory species are now underway.[52-54]

Finally, other data suggest that the role of movement in the sleep process in humans is not straightforward. Our review of the literature found no consistent association between moderately elevated MT and sleep impairment. For example, children diagnosed with attention-deficit-hyperactivity disorder can exhibit elevated MT without corresponding impairment of sleep initiation or maintenance.[55-57] Reduced MT has been reported in normal aging, a phase of life generally accompanied by reduced sleep quality,[58] and in "near-miss" sudden infant death syndrome.[59] These examples hint at additional determinants of sleep movement above and beyond those considered here.

## ACKNOWLEDGMENTS

This research was funded by a Department of Veterans Affairs Merit Review grant to the first author and received logistical support from the National Center for PTSD and the Research and Psychology Services of the Veterans Affairs Palo Alto Health Care System. The authors also wish to thank Ned J. Arsenault for manual scoring of the sleep data.

## REFERENCES

1. Kessler RC, McGonagle KA, Zhao S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Arch Gen Psychiatry 1994;51:8-19.
2. Leskin GA, Woodward SH, Sheikh JI. Nightmares and sleep disturbance in patients with co-morbid PTSD and panic disorder: Findings from the National Comorbidity Survey. 16th Annual Meeting of the International Society for Traumatic Stress Studies. San Antonio, TX.; 2000.
3. Leskin GA, Woodward SH, Young HE, Sheikh JI. Effects of comorbid diagnoses on sleep disturbance in PTSD. Journal of Psychiatric Research; in press.
4. Charney DS, Woods SW, Goodman WK, Heninger GR. Neurobiological mechanisms of panic anxiety: biochemical and behavioral correlates of yohimbine-induced panic attacks. Am J Psychiatry 1987;144:1030-6.
5. Charney DS, Woods SW, Krystal JH, Nagy LM, Heninger GR. Noradrenergic neuronal dysregulation in panic disorder: the effects of intravenous yohimbine and clonidine in panic disorder patients. Acta Psychiatr Scand 1992;86:273-82.
6. Southwick SM, Krystal JH, Morgan CA, et al. Abnormal noradrenergic function in posttraumatic stress disorder. Arch Gen Psychiatry 1993;50:266-74.
7. Bremner JD, Krystal JH, Southwick SM, Charney DS. Noradrenergic mechanisms in stress and anxiety: I. Preclinical studies.

Synapse 1996;23:28-38.
8. Bremner JD, Krystal JH, Southwick SM, Charney DS. Noradrenergic mechanisms in stress and anxiety: II. Clinical studies. Synapse 1996;23:39-51.
9. Mellman TA, Davis GC. Combat-related flashbacks in posttraumatic stress disorder: phenomenology and similarity to panic attacks. J Clin Psychiatry 1985;46:379-82.
10. Freed S, Craske MG, Greher MR. Nocturnal panic and trauma. Depression & Anxiety 1999;9:141-5.
11. Mellman TA, Uhde TW. Electroencephalographic sleep in panic disorder. A focus on sleep- related panic attacks. Arch Gen Psychiatry 1989;46:178-84.
12. Stein MB, Chartier M, Walker JR. Sleep in nondepressed patients with panic disorder: I. Systematic assessment of subjective sleep quality and sleep disturbance. Sleep 1993;16:724-6.
13. Neylan TC, Marmar CR, Metzler TJ, et al. Sleep disturbances in the Vietnam generation: findings from a nationally representative sample of male Vietnam veterans. Am J Psychiatry 1998;155:929-33.
14. Hurwitz TD, Mahowald MW, Kuskowski M, Engdahl BE. Polysomnographic sleep is not clinically impaired in Vietnam combat veterans with chronic posttraumatic stress disorder. Biol Psychiatry 1998;44:1066-73.
15. Uhde TW. Anxiety disorders. In: Kryger MH, Roth T, Dement WC, eds. Principles and practice of sleep medicine. 3rd ed. Philadelphia: WB Saunders; 2000:1123-39.
16. Kulka RA. The national Vietnam veterans readjustment study: tables of findings and technical appendices New York: Brunner/Mazel; 1990 Brunner/Mazel psychosocial stress series; no. 20.
17. Neylan TC, Marmar CR, Metzler TJ, et al. Sleep disturbances in the Vietnam generation: findings from a nationally representative sample of male Vietnam veterans. Am J Psychiatry 1998;155:929-33.
18. Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB. Posttraumatic stress disorder in the National Comorbidity Survey. Arch Gen Psychiatry 1995;52:1048-60.
19. Blake DD, Weathers FW, Nagy LM, et al. The development of a Clinician-Administered PTSD Scale. J Traum Stress 1995;8:75-90.
20. Stegman WK, Stewart LP, Woodward SH, Arsenault NJ, Drescher K. Who enters biological studies of PTSD? Evidence for selection bias. Annual Meeting of the International Society for Traumatic Stress Studies. San Antonio, Texas; 2000.
21. Spitzer RL, Williams B, Gibbon M, First M. Structured clinical interview for the DSM-III-R - Patient Edition (SCID-P). Biometrics Res; 1990.
22. Woodward SH, Arsenault NJ, Santerre C, Michele G, Stewart L, Stegman W. Polysomnographic characteristics of trauma-related nightmares. Sleep. 2000;23(Abstract Supplement #2):356.
23. Rechtschaffen A, Kales A. A manual of standardized terminology, techniques and scoring system for sleep stages of suman subjects. Los Angeles: Brain Information Service/Brain Research Institute/University of California; 1968.
24. Horne JA, Pankhurst FL, Reyner LA, Hume K, Diamond ID. A field study of sleep disturbance: effects of aircraft noise and other factors on 5,742 nights of actimetrically monitored sleep in a large subject sample. Sleep 1994;17:146-59.
25. Lavie P, Hertz G. Increased sleep motility and respiration rates in combat neurotic patients. Biol Psychiatry 1979;14:983-7.
26. Ross RJ, Ball WA, Sullivan KA, Caroff SN. Sleep disturbance as the hallmark of posttraumatic stress disorder. Am J Psychiatry 1989;146:697-707.
27. Aaronson ST, Rashed S, Biber MP, Hobson JA. Brain state and body position. A time-lapse video study of sleep. Arch Gen Psychiatry 1982;39:330-5.
28. Nicholson PW, Leeman AL, O'Neill CJ, et al. Pressure sores: effect of Parkinson's disease and cognitive function on spontaneous movement in bed. Age Ageing 1988;17:111-5.
29. Wilde-Frenz J, Schulz H. Rate and distribution of body movements during sleep in humans. Percept Mot Skills 1983;56:275-83.
30. Middelkoop HA, Van Hilten BJ, Kramer CG, Kamphuisen HA. Actigraphically recorded motor activity and immobility across sleep cycles and stages in healthy male subjects. J Sleep Res 1993;2:28-33.
31. Ross RJ, Ball WA, Dinges DF, et al. Motor dysfunction during sleep in posttraumatic stress disorder. Sleep 1994;17:723-32.
32. Roy-Byrne PP, Uhde TW, Post RM. Effects of one night's sleep deprivation on mood and behavior in panic disorder. Patients with panic disorder compared with depressed patients and normal controls. Arch Gen Psychiatry 1986;43:895-9.
33. Hauri PJ, Friedman M, Ravaris CL. Sleep in patients with spontaneous panic attacks. Sleep 1989;12:323-37.
34. Uhde TW, Roy-Byrne P, Gillin JC, et al. The sleep of patients with panic disorder: a preliminary report. Psychiatry Res 1984;12:251-9.
35. Clark DB, Taylor CB, Hayward C, et al. Motor activity and tonic heart rate in panic disorder. Psychiatry Res 1990;32:45-53.
36. LeDoux J. Fear and the brain: where have we been, and where are we going? Biol Psychiatry 1998;44:1229-38.
37. Antoniadis EA, McDonald RJ. Amygdala, hippocampus and discriminative fear conditioning to context. Behav Brain Res 2000;108:1-19.
38. Bevins RA, McPhee JE, Rauhut AS, Ayres JJ. Converging evidence for one-trial context fear conditioning with an immediate shock: importance of shock potency. J Exp Psychol Anim Behav Process 1997;23:312-24.
39. Phillips RG, LeDoux JE. Differential contribution of amygdala and hippocampus to cued and contextual fear conditioning. Behav Neurosci 1992;106:274-85.
40. Germain A, Nielsen T, Barbier S, Saucier S. Sleep-related markers of idiopathic and PTSD nightmare sufferers: Nighttime awakenings vs. leg movements in sleep. Sleep 2001;24:A354.
41. Woodward SH, Arsenault NJ, Murray C, Bliwise DL. Laboratory sleep correlates of nightmare complaint in PTSD inpatients. Biol Psychiatry 2000;48:1081-7.
42. Mellman TA, Kulick-Bell R, Ashlock LE, Nolan B. Sleep events among veterans with combat-related posttraumatic stress disorder. Am J Psychiatry 1995;152:110-5.
43. Hefez A, Metz L, Lavie P. Long-term effects of extreme situational stress on sleep and dreaming. Am J Psychiatry 1987;144:344-7.
44. Lavie P, Katz N, Pillar G, Zinger Y. Elevated awaking thresholds during sleep: characteristics of chronic war-related posttraumatic stress disorder patients. Biol Psychiatry 1998;44:1060-5.
45. Dagan Y, Zinger Y, Lavie P. Actigraphic sleep monitoring in posttraumatic stress disorder (PTSD) patients. J Psychosom Res 1997;42:577-81.
46. Sadeh A, Sharkey KM, Carskadon MA. Activity-based sleep-wake identification: an empirical test of methodological issues. Sleep 1994;17:201-7.
47. Jean-Louis G, Mendlowicz MV, Gillin JC, et al. Sleep estimation from wrist activity in patients with major depression. Physiol Behav 2000;70:49-53.
48. Woodward SH. Neurobiological perspectives on sleep in PTSD. In: Friedman M, Charney DS, Deutch A, eds. Neurobiological and clinical consequences of stress: from normal adaptation to PTSD. Philadelphia: Lippincott-Raven Publishers; 1995:315-34.
49. Benca RM, Obermeyer WH, Shelton SE, Droster J, Kalin NH. Effects of amygdala lesions on sleep in rhesus monkeys. Brain Res 2000;879:130-8.
50. Bremner JD, Staib LH, Kaloupek D, Southwick SM, Soufer R, Charney DS. Neural correlates of exposure to traumatic pictures and sound in Vietnam combat veterans with and without posttraumatic stress disorder: a positron emission tomography study. Biol

Psychiatry 1999;45:806-16.
51. Rauch SL, Whalen PJ, Shin LM, et al. Exaggerated amygdala response to masked facial stimuli in posttraumatic stress disorder: a functional MRI study. Biol Psychiatry 2000;47:769-76.
52. Morrison AR, Sanford LD, Ross RJ. The amygdala: a critical modulator of sensory influence on sleep. Biol Signals Recept 2000;9:283-96.
53. Deboer T, Sanford LD, Ross RJ, Morrison AR. Effects of electrical stimulation in the amygdala on ponto-geniculo-occipital waves in rats. Brain Res 1998;793:305-10.
54. Sanford LD, Tejani-Butt SM, Ross RJ, Morrison AR. Amygdaloid control of alerting and behavioral arousal in rats: involvement of serotonergic mechanisms. Arch Ital Biol 1995;134:81-99.
55. Busby K, Firestone P, Pivik RT. Sleep patterns in hyperkinetic and normal children. Sleep 1981;4:366-83.
56. Corkum P, Tannock R, Moldofsky H. Sleep disturbances in children with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry 1998;37:637-46.
57. Konofal E, Lecendreux M, Bouvard MP, Mouren-Simeoni MC. High levels of nocturnal activity in children with attention-deficit hyperactivity disorder: a video analysis. Psychiatry Clin Neurosci 2001;55:97-103.
58. Hume KI, Van F, Watson A. A field study of age and gender differences in habitual adult sleep. J Sleep Res 1998;7:85-94.
59. Guilleminault C, Coons S. Near miss sudden infant death infants: a summary of findings (1972-1981). Electroencephalogr Clin Neurophysiol Suppl 1982;36:641-51.

## ABBREVIATIONS

PTSD - posttraumatic stress disorder; PD - panic disorder; MDD - major depressive disorder; ETOH - alcohol abuse/dependence; SUBS - non-alcohol substance abuse/dependence; NREM - non rapid-eye-movement sleep; REM - rapid-eye-movement sleep; DSM-IV - Diagnostic and Statistical Manual, Fourth Revision; CAPS - Clinician Administered PTSD Scale; SCID - Structured Clinical Interview for the DSM-IV; MISS - Mississippi Scale for Combat-Related PTSD; BDI - Beck Depression Inventory; CES - Combat Exposure Scale; EEG - electroencephalogram; EMG - electromyogram; ECG - electrocardiogram; EOG - electrooculogram; ANOVA - analysis of variance; MT - movement time; n.s. - not statistically significant; p - probability of Type I inferential error; r - Pearson's r statistic; rho - Spearman's rho statistic